REMARKS

Claims 3, 6, 13, 30-58, 63-64, and 88-91 have been canceled without prejudice. Claims 1, 9-11, 14, and 59 have been amended. Support for the claim amendments can be found throughout the specification (e.g., page 31, lines 18-23; and Tables 6-7 on pages 98-103). No new matter has been introduced and no new issue has been raised. The amendments have been made solely to expedite allowance. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants note that the Examiner has withdrawn the previous rejection under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) (citing Venter et al.). However, the Examiner has cited new art for claim rejections.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claim Objections

Claim 14 is objected to as allegedly reciting non-elected subject matter. Applicants respectfully disagree. Solely to expedite prosecution of the application, Applicants have amended claim 14 to include the elected species sequence (SEQ ID NO: 231).

Applicants reiterate that independent claim 1 is a generic claim linking elected and non-elected species. Pursuant to MPEP 809.04, "[i]f a linking claim is allowed, the examiner must thereafter examine species if the linking claim is generic thereto, or he or she must examine the claims to the non-elected inventions that are linked to the elected invention by such allowed linking claim." Applicants respectfully request reconsideration and withdrawal of this objection.

Claim Rejections under 35 USC § 102(b) or 35 USC § 103(a)

Claims 1, 3, 5-7, 9-11, 13, 16, and 59 are rejected under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) as being anticipated by or obvious over Bennett et al. (Patent No. 6,277,640). Applicants traverse this rejection to the extent it is maintained over the claims as amended.

Solely to expedite prosecution, Applicants have amended independent claims 1 and 59 to more particularly point out certain technical features (structural and functional) of the nucleic acid compound. Support for the claim amendments can be found throughout the specification (e.g., page 31, lines 18-23; and Tables 6-7 on pages 98-103). For example, claim 1 as amended recites an isolated nucleic acid compound comprising a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell, wherein the nucleic acid compound is an antisense nucleic acid compound comprising one or more modified backbone or base moieties, and wherein the modified antisense nucleic acid comprises at least one 2'-O-alkylated ribonucleotide.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Bennett et al. fail to satisfy the criteria for anticipating the present invention. Bennett et al. describe antisense compounds for modulating the expression of Her-3. However, Bennett et al. do **not** teach or suggest compounds for decreasing expression of EphB4. More specifically, Bennett et al. fail to teach or suggest an antisense nucleic acid compound comprising a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. The SEQ ID cited by the Examiner in the attached sequence alignment (namely SEQ ID NO: 94) does not have the technical features as recited in amended claim 1 or 59. Accordingly, Bennett et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Bennett et al.

Applicants further submit that Bennett et al. do not render obvious the instant claims and note that pursuant to MPEP 2142, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the

reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The instant claims relate to nucleic acid compounds for decreasing expression of EphB4, whereas Bennett et al. are concerned with modulation of expression of Her-3, a molecule that is distinct from EphB4. Indeed, Bennett et al. are absolutely silent on EphB4 as a target for antisense compounds, let alone antisense compounds that comprise a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In the absence of any suggestion in the cited art that EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to design EphB4 targeted nucleic acids as claimed in this application. Further, there is no reasonable expectation of success for a skilled artisan to arriving at the claimed invention.

In view of the above, Bennett et al. do not render obvious the instant claims as amended. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 USC § 102(e) or 35 USC § 103(a)

Claims 1, 3, 5-8, 10-11, 13, 16, and 59 are rejected under 35 U.S.C. § 102(e) or 35 U.S.C. § 103(a) as being anticipated by or obvious over Khvorova et al. (US 2005/0246794). Applicants traverse this rejection as it is maintained over the claims as amended.

Applicants contend that Khvorova et al. fail to satisfy the criteria for anticipating the present invention. Khvorova et al. describe methods for increasing siRNA efficacy. However, Khvorova et al. do **not** teach or suggest compounds for decreasing expression of EphB4. More specifically, Khvorova et al. fail to teach or suggest an antisense nucleic acid compound comprising a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4

transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. The SEQ ID cited by the Examiner in the attached sequence alignment (namely SEQ ID NO: 4253) does not have the technical features as recited in amended claim 1 or 59. Accordingly, Khvorova et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Khvorova et al.

Applicants further submit that Khvorova et al. do not render obvious the instant claims. The instant claims relate to antisense nucleic acid compounds for decreasing expression of EphB4, whereas Khvorova et al. are merely concerned with methods for increasing siRNA efficacy. Indeed, Khvorova et al. are absolutely silent on EphB4 as a target for gene expression inhibition, let alone antisense compounds that comprise a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In the absence of any suggestion in the cited art that EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to design EphB4-targeted nucleic acids as claimed in this application. Further, there is no reasonable expectation of success for a skilled artisan to arriving at the claimed invention.

In view of the above, Khvorova et al. do not render obvious the instant claims as amended. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 USC § 102(e) or 35 USC § 103(a)

Claims 1, 3, 5-11, 13, and 59 are rejected under 35 U.S.C. § 102(e) or 35 U.S.C. § 103(a) as being anticipated by or obvious over Robbins et al. (Patent No: 6,770,633). Applicants traverse this rejection as it is maintained over the claims as amended.

Applicants contend that Robbins et al. fail to satisfy the criteria for anticipating the present invention. Robbins et al. describe methods for treating proliferating eye and skin diseases, in particular, by use of ribozymes in this treatment. However, Robbins et al. do **not** teach or suggest compounds for decreasing expression of EphB4. More specifically, Robbins et al. fail to teach or suggest an antisense nucleic acid compound comprising a nucleotide sequence of between 20 and

35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In fact, the SEQ IDs cited by the Examiner in the attached sequence alignment (namely SEQ ID NOs: 72 and 73) do not have the technical features as recited in amended claim 1 or 59. Accordingly, Robbins et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Robbins et al.

Applicants further submit that Robbins et al. do not render obvious the instant claims. The instant claims relate to antisense nucleic acid compounds for decreasing expression of EphB4, whereas Robbins et al. are concerned with methods of treating proliferative eye disease using ribozymes. Indeed, Robbins et al. are absolutely silent on EphB4 as a target for gene expression inhibition, let alone antisense compounds that comprise a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In the absence of any suggestion in the cited art that EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4-targeted nucleic acids as claimed in this application. Further, there is no reasonable expectation of success for a skilled artisan to arriving at the claimed invention.

In view of the above, Robbins et al. do not render obvious the instant claims as amended. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 USC § 103

Claims 1, 3, 5-8, 10-11, 13-14, 16, and 59 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Miyagishi et al. (Oligonucleotides 2003, 13: 325-333), Promega (siRNA Designer Version 1.1, May 2003, www.promega.com), and Khvorova et al. Applicants traverse this rejection to the extent it is maintained over the claims as amended.

Applicants contend that the cited references (Miyagishi et al., Promega, and Khvorova et al.) fail to satisfy the criteria for rendering obvious independent claims 1 and 59 as amended. These

three cited references are concerned with siRNA molecules for silencing genes other than EphB4. The cited references, singly or in combination, do **not** teach or suggest an antisense compounds that comprise a nucleotide sequence of between 20 and 35 nucleotides which is complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In the absence of any suggestion in the cited art that antisense molecules should be made for decreasing EphB4 gene expression, one of skill in the art would not have been motivated to make EphB4 antisense molecules as claimed in this application. Further, there is no reasonable expectation of success for a skilled artisan to arriving at the claimed invention.

In view of the above, Applicants submit that all claims depending from claim 1 or 59 are not obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance. Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **VASG-P01-001** from which the undersigned is authorized to draw.

Dated: September 28, 2007

Respectfully submitted,

By _____

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